5 <u>CLAIMS</u>

1. A method of treating or preventing chronic organ transplant rejection in a mammal, including a human, comprising administering to said mammal an amount of a compound of the formula

$$R^1$$
 R^2 R^3 R^3

or the pharmaceutically acceptable salt thereof; wherein

R1 is a group of the formula

wherein y is 0, 1 or 2;

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 R^4 is selected from the group consisting of hydrogen, (C_1-C_6) alkyl, (C_1-C_6) alkylsulfonyl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl wherein the alkyl, alkenyl and alkynyl groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C_1-C_4) alkoxy, (C_1-C_6) acyloxy, (C_1-C_6) alkylamino, $((C_1-C_6)$ alkyl)₂amino, cyano, nitro, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl or (C_1-C_6) acylamino; or R^4 is (C_3-C_{10}) cycloalkyl wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C_1-C_6) acyloxy, (C_1-C_6) acylamino, (C_1-C_6) alkyl)₂amino, cyano, cyano (C_1-C_6) alkyl, trifluoromethyl (C_1-C_6) alkyl, nitro, nitro (C_1-C_6) alkyl or (C_1-C_6) acylamino;

 R^5 is (C_2-C_9) heterocycloalkyl wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, halo, (C_1-C_6) acyl, (C_1-C_6) alkylamino, amino (C_1-C_6) alkyl, (C_1-C_6) alkoxy-CO-NH, (C_1-C_6) alkylamino-CO-, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, (C_1-C_6) alkylamino, amino (C_1-C_6) alkyl, hydroxy (C_1-C_6) alkyl, (C_1-C_6) alkoxy (C_1-C_6) alkyl, (C_1-C_6) alkyl, nitro, cyano (C_1-C_6) alkyl, halo (C_1-C_6) alkyl, nitro (C_1-C_6) alkyl, trifluoromethyl, trifluoromethyl (C_1-C_6) alkyl, (C_1-C_6) acylamino, (C_1-C_6) acylamino (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) alkyl, amino (C_1-C_6) acyl (C_1-C_6) alkyl, (C_1-C_6) alkylamino (C_1-C_6) acyl, $((C_1-C_6)$ alkyl) $((C_1-C_6)$ al

CO- (C_1-C_6) alkyl, (C_1-C_6) alkyl- $S(O)_m$, $R^{15}R^{16}NS(O)_m$, $R^{15}R^{16}NS(O)_m$ (C_1-C_6)alkyl, $R^{15}S(O)_m R^{16}N$, $R^{15}S(O)_m R^{16}N$ (C_1-C_6)alkyl wherein m is 0, 1 or 2 and R^{15} and R^{16} are each independently selected from hydrogen or (C_1-C_6)alkyl; or a group of the formula

$$(CR^{6}R^{7})_{a} \qquad (X)_{b} \qquad (CR^{9}R^{10})_{d} \qquad (Y)_{e} \qquad f \qquad (Z)_{g} \qquad R^{12}$$

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wherein a is 0, 1, 2, 3 or 4;

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b, c, e, f and g are each independently 0 or 1; d is 0, 1, 2, or 3;

X is $S(O)_n$ wherein n is 0, 1 or 2; oxygen, carbonyl or -C(=N-cyano)-;

Y is $S(O)_n$ wherein n is 0, 1 or 2; or carbonyl; and

Z is carbonyl, C(O)O-, C(O)NR- or $S(O)_n$ wherein n is 0, 1 or 2;

 R^6 , R^7 , R^8 , R^9 , R^{10} and R^{11} are each independently selected from the group consisting of hydrogen or (C_1-C_6) alkyl optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C_1-C_6) acyloxy, (C_1-C_6) acylamino, (C_1-C_6) alkylamino, (C_1-C_6) alkyl $_2$ amino, cyano, cyano (C_1-C_6) alkyl, trifluoromethyl (C_1-C_6) alkyl, nitro, nitro (C_1-C_6) alkyl or (C_1-C_6) acylamino;

R¹² is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, (C₁trifluoromethyl(C_1 - C_6)alkyl, (C_1 - C_6)alkoxy, halo, (C_1-C_6) acyl, $(C_1 C_6$)alkylamino, ((C_1 - C_6)alkyl)₂ amino, amino(C_1 - C_6)alkyl, (C_1 - C_6)alkoxy-CO-NH, (C_1 - C_6)alkylamino-CO-, (C_2 - C_6)alkenyl, (C_2 - C_6) alkynyl, (C_1 - C_6)alkylamino, hydroxy(C_1 - C_6)alkyl, (C_1-C_6) alkoxy (C_1-C_6) alkyl, (C_1-C_6) acyloxy (C_1-C_6) alkyl, nitro, cyano (C_1-C_6) alkyl C₆)alkyl, halo(C₁-C₆)alkyl, nitro(C₁-C₆)alkyl, trifluoromethyl, trifluoromethyl(C₁-C₆)alkyl, (C₁-C₆)acylamino, (C₁-C₆)acylamino(C₁-C₆)alkyl, (C_1-C_6) alkoxy $(C_1 C_6$)acylamino, amino(C_1 - C_6)acyl, amino(C_1 - C_6)acyl(C_1 - C_6)alkyl, (C_1 - C_6)alkylamino(C_1 - C_6)acyl, $((C_1-C_6)alkyl)_2$ amino $(C_1-C_6)acyl$, $R^{15}R^{16}N-CO-O-$, $R^{15}R^{16}N-CO-(C_1-C_6)alkyl$, $R^{15}C(O)NH$, $R^{15}OC(O)NH$, $R^{15}NHC(O)NH$, $(C_1-C_6)alkyl-S(O)_m$, $(C_1-C_6)alkyl-S(O)_m$ - $R^{15}R^{16}NS(O)_m$, $R^{15}R^{16}NS(O)_m$ (C₁-C₆)alkyl, $R^{15}S(O)_m$ $R^{16}N$. (C₁-C₆)alkyl, $R^{15}S(O)_mR^{16}N(C_1-C_6)$ alkyl wherein m is 0, 1 or 2 and R^{15} and R^{16} are each independently selected from hydrogen or (C₁-C₆)alkyl;

R² and R³ are each independently selected from the group consisting of 5 hydrogen, deuterium, amino, halo, hydoxy, nitro, carboxy, (C2-C6)alkenyl, (C2-C₆)alkynyl, trifluoromethyl, trifluoromethoxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₃-C₁₀)cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally substittued by one to three groups selected from halo, hydroxy, carboxy, amino (C₁-C₆)alkylthio, (C_1-C_6) alkylamino, $((C_1-C_6)$ alkyl)₂amino, (C_5-C_9) heteroaryl, (C_2-C_9) heterocycloalkyl, 10 (C₃-C₉)cycloalkyl or (C₆-C₁₀)aryl; or R² and R³ are each independently (C₃- C_{10})cycloalkyl, (C_3-C_{10}) cycloalkoxy, (C_1-C_6) alkylamino, $((C_1-C_6)$ alkyl)₂amino, (C_6-C_6) alkyl (C₁-C₆)alkylthio, (C₆-C₁₀)arylthio, (C₁-C₆)alkylsulfinyl, C₁₀)arylamino, C₁₀)arylsulfinyl, (C₁-C₆)alkylsulfonyl, (C₆-C₁₀)arylsulfonyl, (C₁-C₆)acyl, (C₁-C₆)alkoxy-CO-NH-, (C₁-C₆)alkyamino-CO-, (C₅-C₉)heteroaryl, (C₂-C₉)heterocycloalkyl or (C₆-15 C₁₀)aryl wherein the heteroaryl, heterocycloalkyl and aryl groups are optionally substituted by one to three halo, (C₁-C₆)alkyl, (C₁-C₆)alkyl-CO-NH-, (C₁-C₆)alkoxy-CO-NH-, (C_1-C_6) alkyl-CO-NH- (C_1-C_6) alkyl, (C_1-C_6) alkoxy-CO-NH- (C_1-C_6) alkyl, (C_1-C_6) C_6)alkoxy-CO-NH-(C_1 - C_6)alkoxy, carboxy, carboxy(C_1 - C_6)alkoxy, carboxy(C_1 - C_6)alkoxy, benzyloxycarbonyl(C_1 - C_6)alkoxy, (C_1 - C_6)alkoxycarbonyl(C_1 - C_6)alkoxy, (C_6 - C_{10})aryl, 20 $(C_6-C_{10})aryl(C_1$ amino. amino(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonylamino, C₆)alkoxycarbonylamino, (C₁-C₆)alkylamino, $((C_1-C_6)alkyl)_2amino,$ $C_6) alkylamino(C_1-C_6) alkyl, \ ((C_1-C_6)alkyl)_2 amino(C_1-C_6) alkyl, \ hydroxy, \ (C_1-C_6)alkoxy,$ carboxy, carboxy(C_1 - C_6)alkyl, (C_1 - C_6)alkoxycarbonyl, (C_1 - C_6)alkoxycarbonyl(C_1 -(C₁-C₆)alkoxy-CO-NH-, (C₁-C₆)alkyl-CO-NH-, (C₅-25 C₆)alkyl, cyano, C₉)heterocycloalkyl, amino-CO-NH-, (C₁-C₆)alkylamino-CO-NH-, ((C₁-C₆)alkyl)₂amino-CO-NH-, (C₆-C₁₀)arylamino-CO-NH-, (C₅-C₉)heteroarylamino-CO-((C₁-C₆)alkyl)₂amino-CO-NH-(C₁-NH-. (C_1-C_6) alkylamino-CO-NH- (C_1-C_6) alkyl, C₆)alkyl, (C₆-C₁₀)arylamino-CO-NH-(C₁-C₆)alkyl, (C₅-C₉)heteroarylamino-CO-NH-(C₁-30 C₆)alkyl, (C₁-C₆)alkylsulfonyl, (C₁-C₆)alkylsulfonylamino, (C₁- C_6)alkylsulfonylamino(C_1 - C_6)alkyl, (C_6 - C_{10})arylsulfonyl, (C_6-C_{10}) arylsulfonylamino, (C₁-C₆)alkylsulfonylamino, (C_6-C_{10}) arylsulfonylamino (C_1-C_6) alkyl, (C₁- C_6)alkylsulfonylamino(C_1 - C_6)alkyl, (C_5 - C_9)heteroaryl or (C_2 - C_9)heterocycloalkyl; effective in treating such a condition.

2. A method according to claim 1, wherein a is 0; b is 1; X is carbonyl; c is 0; d is 0; e is 0; f is 0; and g is 0.

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3. A method according to claim 1, wherein a is 0; b is 1; X is carbonyl; c is 0; d is 1; e is 0; f is 0, and g is 0.

- 5 4. A method according to claim 1, wherein a is 0; b is 1; X is carbonyl; c is 1; d is 0; e is 0; f is 0; and g is 0.
 - 5. A method according to claim 1, wherein a is 0; b is 1; X is C(=N=cyano)-; c is 1; d is 0; e is 0; f is 0; and g is 0.
- 6. A method according to claim 1, wherein a is 0; b is 0; c is 0; d is 0; e is 0; f is 0; g is 1; and Z is -C(O)-O-.
 - 7. A method according to claim 1, wherein a is 0; b is 1; X is $S(O)_n$; n is 2; c is 0; d is 0; e is 0; f is 0; and g is 0.
 - 8. A method according to claim 1, wherein a is 0; b is 1; X is S(O)_n; n is 2; c is 0; d is 2; e is 0; f is 1; g is 1; and Z is carbonyl.
- 9. A method according to claim 1, wherein a is 0; b is 1; X is S(O)_n; n is 2; c is 0; d is 2; e is 0; f is 1; and g is 0.
 - 10. A method according to claim 1, wherein a is 0; b is 1; X is carbonyl; c is 1; d is 0; e is 1; Y is S(O)_n; n is 2; f is 0; and g is 0.
- 11. A method according to claim 1, wherein a is 0; b is 1; X is $S(O)_n$; n is 20 2; c is 1; d is 0; e is 0; f is 0; and g is 0.
 - 12. A method according to claim 1, wherein R^{12} is cyano, trifluoromethyl, (C_1-C_6) alkyl, trifluoromethyl (C_1-C_6) alkyl, (C_1-C_6) alkylamino, $((C_1-C_6)$ alkyl) $_2$ amino, (C_2-C_6) alkynyl, cyano (C_1-C_6) alkyl, (C_1-C_6) alkyl- $S(O)_m$ wherein m is 0, 1 or 2.
- 13. A method according to claim 1, wherein said compound is selected from the group consisting of:

Methyl-[4-methyl-1-(propane-1-sulfonyl)-piperidin-3-yl]-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amine;

- 4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidine-1-carboxylic acid methyl ester;
- 30 3,3,3-Trifluoro-1-{4-methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl}-propan-1-one;
 - 4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidine-1-carboxylic acid dimethylamide;
- ({4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidine-1-35 carbonyl}-amino)-acetic acid ethyl ester;
 - 3-{4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl}-3-oxo-propionitrile;

5 3,3,3-Trifluoro-1-{4-methyl-3-[methyl-(5-methyl-7H-pyrrolo[2,3-d]pyrimidin-4yl)-amino]-piperidin-1-yl}-propan-1-one; 1-{4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidin-1-yl}but-3-yn-1-one; 1-{3-[(5-Chloro-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-methyl-amino]-4-methylpiperidin-1-yl}-propan-1-one; 10 1-{3-[(5-Fluoro-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-methyl-amino]-4-methylpiperidin-1-yl}-propan-1-one; N-cyano-4-methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-N'propyl-piperidine-1-carboxamidine; 15 N-cyano-4,N',N'-Trimethyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]piperidine-1-carboxamidine; Methyl-[(3R,4R)-4-methyl-1-(propane-1-sulfonyl)-piperidin-3-yl]-(7Hpyrrolo[2,3-d]pyrimidin-4-yl)-amine; (3R,4R)-)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-20 piperidine-1-carboxylic acid methyl ester; 3,3,3-Trifluoro-1-{(3R,4R)-4-methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4yl)-amino]-piperidin-1-yl}-propan-1-one; (3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]piperidine-1-carboxylic acid dimethylamide; 25 {(3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidine-1-carbonyl}-amino)-acetic acid ethyl ester; 3-{(3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]piperidin-1-yl}-3-oxo-propionitrile; 3,3,3-Trifluoro-1-{(3R,4R)-4-methyl-3-[methyl-(5-methyl-7H-pyrrolo[2,3-30 d]pyrimidin-4-yl)-amino]-piperidin-1-yl}-propan-1-one; 1-{(3R,4R)-4-Methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]piperidin-1-yl}-but-3-yn-1-one; 1-{(3R,4R)-3-[(5-Chloro-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-methyl-amino]-4methyl-piperidin-1-yl}-propan-1-one; 35 1-{(3R,4R)-3-[(5-Fluoro-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-methyl-amino]-4methyl-piperidin-1-yl}-propan-1-one; (3R,4R)-N-cyano-4-methyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-N'-propyl-piperidine-1-carboxamidine; and

(3R,4R)-N-cyano-4,N',N'-Trimethyl-3-[methyl-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-amino]-piperidine-1-carboxamidine.

14. A method of treating or preventing acute organ transplant rejection in a mammal, including a human, comprising administering to said mammal an amount of a compound of the formula

$$\begin{array}{c|c}
R^1 & R^2 \\
N & N \\
N & H
\end{array}$$

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or the pharmaceutically acceptable salt thereof; wherein

R¹ is a group of the formula

$$R^4$$
 $(CH_2)_y$

wherein y is 0, 1 or 2;

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 R^4 is selected from the group consisting of hydrogen, (C_1-C_6) alkyl, (C_1-C_6) alkylsulfonyl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl wherein the alkyl, alkenyl and alkynyl groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C_1-C_4) alkoxy, (C_1-C_6) acyloxy, (C_1-C_6) alkylamino, $((C_1-C_6)$ alkyl)₂amino, cyano, nitro, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl or (C_1-C_6) acylamino; or R^4 is (C_3-C_{10}) cycloalkyl wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C_1-C_6) acyloxy, (C_1-C_6) acylamino, (C_1-C_6) alkyl)₂amino, cyano, cyano (C_1-C_6) alkyl, trifluoromethyl (C_1-C_6) alkyl, nitro, nitro (C_1-C_6) alkyl or (C_1-C_6) acylamino;

 R^5 is (C_2-C_9) heterocycloalkyl wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, halo, (C_1-C_6) acyl, (C_1-C_6) alkylamino, amino (C_1-C_6) alkyl, (C_1-C_6) alkylamino-CO-, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, (C_1-C_6) alkylamino, amino (C_1-C_6) alkyl, hydroxy (C_1-C_6) alkyl, (C_1-C_6) alkoxy (C_1-C_6) alkyl, nitro, cyano (C_1-C_6) alkyl, halo (C_1-C_6) alkyl, nitro (C_1-C_6) alkyl, trifluoromethyl, trifluoromethyl (C_1-C_6) alkyl, (C_1-C_6) acylamino, (C_1-C_6) acylamino, amino (C_1-C_6) acylamino, amino (C_1-C_6) acyl (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) acylamino, amino (C_1-C_6) acyl (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) acylamino, amino (C_1-C_6) acyl (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) acylamino, amino (C_1-C_6) acyl (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) acylamino, amino (C_1-C_6) acyl (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) acylamino, amino (C_1-C_6) acyl (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) acylamino, amino (C_1-C_6) acyl (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) acylamino, amino (C_1-C_6) acyl (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) acylamino, amino (C_1-C_6) acylamino, amino (C_1-C_6) alkyl, (C_1-C_6) alkyl

5 C₆)alkylamino(C₁-C₆)acyl, ((C₁-C₆)alkyl)₂amino(C₁-C₆)acyl, R¹⁵R¹⁶N-CO-O-, R¹⁵R¹⁶N-CO-(C₁-C₆)alkyl, (C₁-C₆)alkyl-S(O)_m, R¹⁵R¹⁶NS(O)_m, R¹⁵R¹⁶NS(O)_m (C₁-C₆)alkyl, R¹⁵S(O)_m R¹⁶N, R¹⁵S(O)_mR¹⁶N(C₁-C₆)alkyl wherein m is 0, 1 or 2 and R¹⁵ and R¹⁶ are each independently selected from hydrogen or (C₁-C₆)alkyl; or a group of the formula

$$(CR^{6}R^{7})_{a}$$
 $(X)_{b}$
 $(CR^{9}R^{10})_{d}$
 $(Y)_{e}$
 $(X)_{g}$
 (X)

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10 wherein a is 0, 1, 2, 3 or 4;

b, c, e, f and g are each independently 0 or 1;

d is 0, 1, 2, or 3;

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X is $S(O)_n$ wherein n is 0, 1 or 2; oxygen, carbonyl or -C(=N-cyano)-;

Y is S(O)_n wherein n is 0, 1 or 2; or carbonyl; and

Z is carbonyl, C(O)O-, C(O)NR- or S(O)_n wherein n is 0, 1 or 2;

 R^6 , R^7 , R^8 , R^9 , R^{10} and R^{11} are each independently selected from the group consisting of hydrogen or (C_1-C_6) alkyl optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C_1-C_6) acyloxy, (C_1-C_6) acylamino, (C_1-C_6) alkyl)₂amino, cyano, cyano (C_1-C_6) alkyl, trifluoromethyl (C_1-C_6) alkyl, nitro, nitro (C_1-C_6) alkyl or (C_1-C_6) acylamino;

R¹² is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, (C₁trifluoromethyl(C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo, (C₁-C₆)acyl, C_6)alkylamino, ((C_1 - C_6)alkyl), amino, amino(C_1 - C_6)alkyl, (C_1 - C_6)alkoxy-CO-NH, (C_1 - C_6)alkylamino-CO-, (C_2 - C_6)alkenyl, (C_2 - C_6) alkynyl, (C_1 - C_6)alkylamino, hydroxy(C_1 - C_6)alkyl, (C_1-C_6) alkoxy (C_1-C_6) alkyl, (C_1-C_6) acyloxy (C_1-C_6) alkyl, nitro, cyano (C_1-C_6) alkyl, nitro, cyan halo(C₁-C₆)alkyl, nitro(C₁-C₆)alkyl, trifluoromethyl, trifluoromethyl(C₁-C₆)alkyl, C₆)alkyl, (C₁-C₆)acylamino, (C_1-C_6) acylamino (C_1-C_6) alkyl, (C_1-C_6) alkoxy $(C_1 C_6$)acylamino, amino(C_1 - C_6)acyl, amino(C_1 - C_6)acyl(C_1 - C_6)alkyl, (C_1 - C_6)alkylamino(C_1 - C_6)acyl, $((C_1-C_6)alkyl)_2$ amino $(C_1-C_6)acyl$, $R^{15}R^{16}N-CO-O-$, $R^{15}R^{16}N-CO-(C_1-C_6)alkyl$, $R^{15}C(O)NH$, $R^{15}OC(O)NH$, $R^{15}NHC(O)NH$, $(C_1-C_6)alkyl-S(O)_m$, $(C_1-C_6)alkyl-S(O)_m$ $R^{15}R^{16}NS(O)_{m}$, $R^{15}R^{16}NS(O)_{m}$ (C₁-C₆)alkyl, $R^{15}S(O)_{m}$ $R^{16}N$, (C₁-C₆)alkyl,

 $R^{15}S(O)_mR^{16}N(C_1-C_6)$ alkyl wherein m is 0, 1 or 2 and R^{15} and R^{16} are each independently selected from hydrogen or (C_1-C_6) alkyl;

R² and R³ are each independently selected from the group consisting of hydrogen, deuterium, amino, halo, hydoxy, nitro, carboxy, (C2-C6)alkenyl, (C2- C_6)alkynyl, trifluoromethyl, trifluoromethoxy, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_3-C_6) alkyl, (C_1-C_6) alkyl, C₁₀)cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally substittued 10 by one to three groups selected from halo, hydroxy, carboxy, amino (C₁-C₆)alkylthio, (C_1-C_6) alkylamino, $((C_1-C_6)$ alkyl)₂amino, (C_5-C_9) heteroaryl, (C_2-C_9) heterocycloalkyl, (C_3-C_9) cycloalkyl or (C_6-C_{10}) aryl; or R^2 and R^3 are each independently (C_3-C_9) C_{10})cycloalkyl, (C_3-C_{10}) cycloalkoxy, (C_1-C_6) alkylamino, $((C_1-C_6)$ alkyl)₂amino, (C_6-C_{10}) cycloalkoxy, (C_6-C_{10}) cycloalkyl, (C_6-C_{10}) cycloalkoxy, (C_6-C_{10}) cycloalkyl, (C_6-C_{10}) cycloalkyl, (C_6-C_{10}) cycloalkyl, (C_6-C_{10}) cycloalkoxy, (C_6-C_{10}) cycloalkyl, (C_6-C_{10}) cyclo 15 C₁₀)arylamino, (C₁-C₆)alkylthio, (C₆-C₁₀)arylthio, (C₁-C₆)alkylsulfinyl, $(C_6 C_{10}$)arylsulfinyl, (C_1-C_6) alkylsulfonyl, (C_6-C_{10}) arylsulfonyl, (C_1-C_6) acyl, (C_1-C_6) alkoxy-CO-NH-, (C₁-C₆)alkyamino-CO-, (C₅-C₉)heteroaryl, (C₂-C₉)heterocycloalkyl or (C₆-C₁₀)aryl wherein the heteroaryl, heterocycloalkyl and aryl groups are optionally substituted by one to three halo, (C₁-C₆)alkyl, (C₁-C₆)alkyl-CO-NH-, (C₁-C₆)alkoxy-CO-NH-, (C_1-C_6) alkyl-CO-NH- (C_1-C_6) alkyl, (C_1-C_6) alkoxy-CO-NH- (C_1-C_6) alkyl, (C_1-C_6) 20 C_6)alkoxy-CO-NH-(C_1 - C_6)alkoxy, carboxy, carboxy(C_1 - C_6)alkyl, carboxy(C_1 - C_6)alkoxy, benzyloxycarbonyl(C_1 - C_6)alkoxy, (C_1 - C_6)alkoxycarbonyl(C_1 - C_6)alkoxy, (C_6 - C_{10})aryl, amino, amino(C₁-C₆)alkyl, (C₁-C₆)alkoxycarbonylamino, (C_6-C_{10}) aryl $(C_1-$ C₆)alkoxycarbonylamino, (C₁-C₆)alkylamino, $((C_1-C_6)alkyl)_2amino,$ (C₁- C_6)alkylamino(C_1 - C_6)alkyl, ((C_1 - C_6)alkyl)₂amino(C_1 - C_6)alkyl, hydroxy, (C_1 - C_6)alkoxy, 25 carboxy(C_1 - C_6)alkyl, (C_1 - C_6)alkoxycarbonyl, (C_1 - C_6)alkoxycarbonyl(C_1 carboxy. C₆)alkyl, (C₁-C₆)alkoxy-CO-NH-, (C₁-C₆)alkyl-CO-NH-, cyano, $(C_5-$ C₉)heterocycloalkyl, amino-CO-NH-, (C₁-C₆)alkylamino-CO-NH-, ((C₁-C₆)alkyl)₂amino-CO-NH-, (C₆-C₁₀)arylamino-CO-NH-, (C₅-C₉)heteroarylamino-CO-NH-, (C_1-C_6) alkylamino-CO-NH- (C_1-C_6) alkyl, ((C₁-C₆)alkyl)₂amino-CO-NH-(C₁-30 C_6)alkyl, (C_6 - C_{10})arylamino-CO-NH-(C_1 - C_6)alkyl, (C_5 - C_9)heteroarylamino-CO-NH-(C_1 -(C₁-C₆)alkylsulfonyl, (C₁-C₆)alkylsulfonylamino, C_6)alkylsulfonylamino(C_1 - C_6)alkyl, (C_6 - C_{10})arylsulfonyl, (C_6 - C_{10})arylsulfonylamino, (C_6-C_{10}) arylsulfonylamino (C_1-C_6) alkyl, (C₁-C₆)alkylsulfonylamino, (C₁- C_6)alkylsulfonylamino(C_1 - C_6)alkyl, (C_5 - C_9)heteroaryl or (C_2 - C_9)heterocycloalkyl; 35

effective in treating such a condition.

15. A pharmaceutical composition for treating or preventing chronic organ transplant rejection in a mammal, including a human, comprising an amount of a compound of the formula

or the pharmaceutically acceptable salt thereof; wherein

R¹ is a group of the formula

wherein y is 0, 1 or 2;

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 R^4 is selected from the group consisting of hydrogen, $(C_1\text{-}C_6)$ alkyl, $(C_1\text{-}C_6)$ alkylsulfonyl, $(C_2\text{-}C_6)$ alkenyl, $(C_2\text{-}C_6)$ alkynyl wherein the alkyl, alkenyl and alkynyl groups are optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, $(C_1\text{-}C_4)$ alkoxy, $(C_1\text{-}C_6)$ acyloxy, $(C_1\text{-}C_6)$ alkylamino, $((C_1\text{-}C_6)$ alkyl) $_2$ amino, cyano, nitro, $(C_2\text{-}C_6)$ alkenyl, $(C_2\text{-}C_6)$ alkynyl or $(C_1\text{-}C_6)$ acylamino; or R^4 is $(C_3\text{-}C_{10})$ cycloalkyl wherein the cycloalkyl group is optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, $(C_1\text{-}C_6)$ acyloxy, $(C_1\text{-}C_6)$ acylamino, $(C_1\text{-}C_6)$ alkyl) $_2$ amino, cyano, cyano $(C_1\text{-}C_6)$ alkyl, trifluoromethyl $(C_1\text{-}C_6)$ alkyl, nitro, nitro $(C_1\text{-}C_6)$ alkyl or $(C_1\text{-}C_6)$ acylamino;

 R^5 is (C_2-C_9) heterocycloalkyl wherein the heterocycloalkyl groups must be substituted by one to five carboxy, cyano, amino, deuterium, hydroxy, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, halo, (C_1-C_6) acyl, (C_1-C_6) alkylamino, amino (C_1-C_6) alkyl, (C_1-C_6) alkoxy-CO-NH, (C_1-C_6) alkylamino-CO-, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, (C_1-C_6) alkylamino, amino (C_1-C_6) alkyl, hydroxy (C_1-C_6) alkyl, (C_1-C_6) alkoxy (C_1-C_6) alkyl, (C_1-C_6) alkyl, nitro, cyano (C_1-C_6) alkyl, halo (C_1-C_6) alkyl, nitro (C_1-C_6) alkyl, trifluoromethyl, trifluoromethyl (C_1-C_6) alkyl, (C_1-C_6) acylamino, (C_1-C_6) acylamino (C_1-C_6) alkyl, (C_1-C_6) alkyl, (C_1-C_6) alkyl, amino (C_1-C_6) acyl (C_1-C_6) alkyl, (C_1-C_6) alkylamino (C_1-C_6) acyl, $((C_1-C_6)$ alkyl) $((C_1-C_6)$ al

R¹⁵S(O)_m R¹⁶N, R¹⁵S(O)_mR¹⁶N(C₁-C₆)alkyl wherein m is 0, 1 or 2 and R¹⁵ and R¹⁶ are each independently selected from hydrogen or (C₁-C₆)alkyl; or a group of the formula

$$(CR^{6}R^{7})_{a} \qquad (X)_{b} \qquad (CR^{9}R^{10})_{d} \qquad (Y)_{e} \qquad (Y)_{e} \qquad (Z)_{g} \qquad (Z)_{g} \qquad (X)_{b} \qquad (X)_{e} \qquad (X)_{g} \qquad (X)$$

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wherein a is 0, 1, 2, 3 or 4;

b, c, e, f and g are each independently 0 or 1;

10 d is 0, 1, 2, or 3;

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X is $S(O)_n$ wherein n is 0, 1 or 2; oxygen, carbonyl or -C(=N-cyano)-;

Y is S(O)_n wherein n is 0, 1 or 2; or carbonyl; and

Z is carbonyl, C(O)O-, C(O)NR- or S(O)_n wherein n is 0, 1 or 2;

 R^6 , R^7 , R^8 , R^9 , R^{10} and R^{11} are each independently selected from the group consisting of hydrogen or (C_1-C_6) alkyl optionally substituted by deuterium, hydroxy, amino, trifluoromethyl, (C_1-C_6) acyloxy, (C_1-C_6) acylamino, (C_1-C_6) alkylamino, (C_1-C_6) alkyl $)_2$ amino, cyano, cyano (C_1-C_6) alkyl, trifluoromethyl (C_1-C_6) alkyl, nitro, nitro (C_1-C_6) alkyl or (C_1-C_6) acylamino;

R¹² is carboxy, cyano, amino, oxo, deuterium, hydroxy, trifluoromethyl, (C₁trifluoromethyl(C_1 - C_6)alkyl, (C_1 - C_6)alkoxy, halo, 20 (C₁-C₆)acyl, C_6)alkylamino, ((C_1 - C_6)alkyl)₂ amino, amino(C_1 - C_6)alkyl, (C_1 - C_6)alkoxy-CO-NH, (C_1 -C₆)alkylamino-CO-, (C₂-C₆)alkenyl, (C₂-C₆) alkynyl, (C₁-C₆)alkylamino, hydroxy(C₁- C_6)alkyl, (C_1-C_6) alkoxy (C_1-C_6) alkyl, (C_1-C_6) acyloxy (C_1-C_6) alkyl, nitro, cyano (C_1-C_6) alkyl, nitro, cyan C₆)alkyl, halo(C_1 - C_6)alkyl, nitro(C_1 - C_6)alkyl, trifluoromethyl, trifluoromethyl(C₁-25 C₆)alkyl, (C₁-C₆)acylamino, (C_1-C_6) acylamino (C_1-C_6) alkyl, (C_1-C_6) alkoxy $(C_1 C_6$)acylamino, amino(C_1 - C_6)acyl, amino(C_1 - C_6)acyl(C_1 - C_6)alkyl, (C_1 - C_6)alkylamino(C_1 - C_6)acyl, $((C_1-C_6)alkyl)_2$ amino $(C_1-C_6)acyl$, $R^{15}R^{16}N-CO-O-$, $R^{15}R^{16}N-CO-(C_1-C_6)alkyl$, $R^{15}C(O)NH$, $R^{15}OC(O)NH$, $R^{15}NHC(O)NH$, $(C_1-C_6)alkyl-S(O)_m$, $(C_1-C_6)alkyl-S(O)_m$ $R^{15}R^{16}NS(O)_m$, $R^{15}R^{16}NS(O)_m$ (C₁-C₆)alkyl, $R^{15}S(O)_m$ $R^{16}N$, (C₁-C₆)alkyl, $R^{15}S(O)_mR^{16}N(C_1-C_6)$ alkyl wherein m is 0, 1 or 2 and R^{15} and R^{16} are each 30 independently selected from hydrogen or (C₁-C₆)alkyl;

R² and R³ are each independently selected from the group consisting of 5 hydrogen, deuterium, amino, halo, hydoxy, nitro, carboxy, (C2-C6)alkenyl, (C2-C₆)alkynyl, trifluoromethyl, trifluoromethoxy, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, (C₃-C₁₀)cycloalkyl wherein the alkyl, alkoxy or cycloalkyl groups are optionally substittued by one to three groups selected from halo, hydroxy, carboxy, amino (C₁-C₆)alkylthio, (C_1-C_6) alkylamino, $((C_1-C_6)$ alkyl)₂amino, (C_5-C_9) heteroaryl, (C_2-C_9) heterocycloalkyl, 10 (C₃-C₉)cycloalkyl or (C₆-C₁₀)aryl; or R² and R³ are each independently (C₃- C_{10})cycloalkyl, (C_3-C_{10}) cycloalkoxy, (C_1-C_6) alkylamino, $((C_1-C_6)$ alkyl)₂amino, (C_6-C_6) C₁₀)arylamino, (C₁-C₆)alkylthio, (C_6-C_{10}) arylthio, (C₁-C₆)alkylsulfinyl, C_{10})arylsulfinyl, (C_1-C_6) alkylsulfonyl, (C_6-C_{10}) arylsulfonyl, (C_1-C_6) acyl, (C_1-C_6) alkoxy-CO-NH-, (C₁-C₆)alkyamino-CO-, (C₅-C₉)heteroaryl, (C₂-C₉)heterocycloalkyl or (C₆-15 C₁₀)aryl wherein the heteroaryl, heterocycloalkyl and aryl groups are optionally substituted by one to three halo, (C₁-C₆)alkyl, (C₁-C₆)alkyl-CO-NH-, (C₁-C₆)alkoxy-CO-NH-, (C_1-C_6) alkyl-CO-NH- (C_1-C_6) alkyl, (C_1-C_6) alkoxy-CO-NH- (C_1-C_6) alkyl, (C_1-C_6) C_6)alkoxy-CO-NH-(C_1 - C_6)alkoxy, carboxy, carboxy(C_1 - C_6)alkyl, carboxy(C_1 - C_6)alkoxy, benzyloxycarbonyl(C_1 - C_6)alkoxy, (C_1 - C_6)alkoxycarbonyl(C_1 - C_6)alkoxy, (C_6 - C_{10})aryl, 20 amino. amino(C₁-C₆)alkyl, (C_1-C_6) alkoxycarbonylamino, $(C_6-C_{10})aryl(C_{1-}$ C₆)alkoxycarbonylamino, (C₁-C₆)alkylamino, $((C_1-C_6)alkyl)_2amino,$ (C₁- C_6)alkylamino(C_1 - C_6)alkyl, ((C_1 - C_6)alkyl)₂amino(C_1 - C_6)alkyl, hydroxy, (C_1 - C_6)alkoxy, carboxy, carboxy(C_1 - C_6)alkyl, (C_1 - C_6)alkoxycarbonyl, (C_1 - C_6)alkoxycarbonyl(C_1 -C₆)alkyl, (C_1-C_6) alkoxy-CO-NH-, (C₁-C₆)alkyl-CO-NH-, 25 cyano, (C₅-C₉)heterocycloalkyl, amino-CO-NH-, (C₁-C₆)alkylamino-CO-NH-, ((C₁-C₆)alkyl)₂amino-CO-NH-, (C₆-C₁₀)arylamino-CO-NH-, (C₅-C₉)heteroarylamino-CO- (C_1-C_6) alkylamino-CO-NH- (C_1-C_6) alkyl NH-. ((C₁-C₆)alkyl)₂amino-CO-NH-(C₁-C₆)alkyl, (C₆-C₁₀)arylamino-CO-NH-(C₁-C₆)alkyl, (C₅-C₉)heteroarylamino-CO-NH-(C₁-30 C₆)alkyl, (C₁-C₆)alkylsulfonyl, (C₁-C₆)alkylsulfonylamino, (C₁- C_6)alkylsulfonylamino(C_1 - C_6)alkyl, (C_6 - C_{10})arylsulfonyl, (C_6 - C_{10})arylsulfonylamino, (C_6-C_{10}) arylsulfonylamino (C_1-C_6) alkyl, (C₁-C₆)alkylsulfonylamino, C_6)alkylsulfonylamino(C_1 - C_6)alkyl, (C_5 - C_9)heteroaryl or (C_2 - C_9)heterocycloalkyl, effective in such disorders or conditions and a pharmaceutically acceptable carrier.